1: Drugs R D. 2006;7(5):312-6.

CpG 7909: PF 3512676, PF-3512676.

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CpG 7909 [PF-3512676] is an immunomodulating synthetic oligonucleotide designed to specifically agonise the Toll-like receptor 9 (TLR9). It is being developed for the treatment of cancer [ProMune] as a monotherapy and in combination with chemotherapeutic agents, and it is also under development as an adjuvant [VaxImmune] for vaccines against cancer and infectious diseases. CpG 7909, acting through the TLR9 receptor present in B cells and plasmacytoid dendritic cells, stimulates human B-cell proliferation, enhances antigen-specific antibody production and induces interferon-alpha production, interleukin-10 secretion and natural killer cell activity. Coley Pharmaceutical Group originally developed CpG 7909 using its CpG DNA technology. In March 2005, Coley granted Pfizer an exclusive global license to develop and commercialise CPG 7909 [ProMune] for the treatment, control and prevention of multiple cancer indications. Coley licensed CpG 7909 [VaxImmune] to Chiron Corporation for adjuvant use with Chiron's prophylactic vaccine candidates against infectious diseases in December 2003. Chiron was acquired by and merged into Novartis in April 2006. In 2002, GlaxoSmithKline (GSK) was granted a worldwide, non-exclusive licence to Coley's CpG immunostimulatory oligonucleotides, including CpG 7909 [VaxImmune], for their use as adjuvants for cancer vaccines. In 2000, Coley entered into a co-exclusive licensing agreement with GSK for the development of therapeutic and prophylactic vaccines against infectious diseases. This licensing agreement included CpG 7909 [VaxImmune] and other CpG-based immunostimulatory oligonucleotides. In September 2004, Coley Pharmaceuticals was awarded a 16.9 million US dollars, 3-year contract from the National Institute of Allergy and Infectious Diseases (NIAID), one of the National Institutes of Health (NIH), to support the development of novel immune-activating drugs for defense against bioterror agents. This contract will be used to expand Coley's proprietary line of TLR Therapeutic products. Together with prior awards, the new contract brings the total committed biodefense funding for Coley to 35 million US dollars. During the first quater of 2006, Pfizer disclosed its intention to develop CpG 7909 for breast cancer. A phase I/II trial in patients with NHL has also been conducted in 24 patients with relapsed or refractory disease at the University of Iowa. Pfizer initiated two international phase III trials under the special protocol assessment (SPA) procedure of the US FDA. These trials are evaluating CpG 7909 in combination with chemotherapy versus chemotherapy alone as a first-line treatment for patients with advanced (stage IIIb or IV) non-small-cell lung cancer (NSCLC). Approximately 800 patients will be enrolled in each trial. The primary endpoint is overall survival time. In 2005, Coley completed a multinational phase IIb trial of CpG 7909 in combination with chemotherapy in 112 patients with NSCLC. The goal of the study was to improve the outcome of standard first-line chemotherapeutic regimens (taxane and platinum) for NSCLC by adding CpG 7909. Coley has been granted 11 US patents, covering key aspects of the company's CpG TLR9 antagonist technologies. Three US patents relating to CpG 7909 and the use of certain oligonucleotides for treating cancer are due to expire in 2014. Coley also has pending US patent applications covering the specific sequence of CpG 7909 and its use to treat cancer, which, if issued, would be expected to expire between 2014 and 2017. In April 2004, Coley received US Patent No. 6,727,230 covering the use of oligonucleotides containing at least one phosphorothioate linkage to stimulate cellular immune responses. In November 2003, Coley received US Patent No. 6,653,292, which protects the use of TLR9-containing oligonucleotides to treat or prevent cancer or to enhance multimodal cancer treatment regimens. In July 2002, Coley received US Patent No. 6,406,705 covering its CpG oligonucleotide immunostimulants for use in combination with conventional adjuvants. In April 2001, Coley was issued with US Patent No. 6,207,646 covering the composition and use of its immune stimulants including CpG 7909. In September 2001, Coley was granted US Patent No. 6,214,806, which expands the coverage on the use of CpG oligonucleotides in the treatment of certain respiratory disorders.